REMARKS

Claims 61, 68, and 81-97 are pending. Claims 61 and 68 are allowed. Claim 61 is amended. Claims 81-101 are added. No new matter is added as a result of these amendments or new claims. The Examiner notes that there is some inconsistency in the spelling of the "IKBKAP" gene in the claims. As suggested by the Examiner, this has been corrected, and the claims only refer to "IKBKAP" as supported by the specification. Claim 61 is amended to recite "IKBKAP" rather than "IKAP."

Support for new claims 81-101

Support for new claims 81-101 can be found throughout the original application as filed. Support for the recitation of location of the FD mutations within the IKBKAP gene, as well as the nucleotide changes associated with those mutations is found at least on pages 3, 7, 9, and 34 of the specification. Further support for the IKBKAP gene, the location of the mutations, and the location of the introns and exons associated with the mutations is found at least in Figures 1 and 6, and on pages 7 and 33 of the specification. Support for detection of the FD mutations using oligonucleotide probes and PCR primers that flank the FD mutations is found in the specification at least on pages 4-5, 12, and 27, and support for kits for detection of FD mutations is provided at least on pages 6 and 32 of the specification. Support for the length of suitable probes and primers of the invention is found on at least pages 13, 27, and 33 of the specification. Support for using complementary probes is found on at least pages 13 and 34 of the specification.

Interview Summary

Applicants thank the Examiner, Carla Myers, for the extreme courtesy of two telephone interviews. Applicants were represented in the interviews by Margaret Brivanlou and Deborah Drazen who attended on February 6, 2007 and February 21, 2007. In the interviews, the Office Action mailed August 28, 2006 and the then pending claims were discussed. Proposed claim amendments relating to the rejections were presented. Applicants' representatives also discussed issues related to benefit to the priority application. No agreement was reached.

Priority

The Examiner indicates that claims 50 and 76, which recite the full length of SEQ ID NO: 1 are not entitled to priority to provisional application 60/260,080 because the application was not filed with a complete set of drawings.

The Examiner states that claims 78 and 80 are not entitled to the filing date of the provisional application 60/260,080 because the application does not disclose the nucleotide sequence of SEQ ID NO: 2 because a reference to a GenBank Accession number constitutes an improper incorporation by reference to essential subject matter because this subject matter is necessary to describe the claimed invention.

Further, the Examiner states that claims 77 and 79 are not entitled to the filing date of the provisional application 60/260,080 because the application does not appear to provide support or the concept of nucleic acids consisting of 16 nucleotides selected from the specific region of exon 19 to exon 20 of SEQ ID NO: 1.

The Examiner states that claim 65 is not entitled to the filing date of the provisional application 60/260,080 because the application does not appear to disclose a kit wherein the

primers of SEQ ID NOs 19 and 23 are used to amplify a region of sufficient size to detect both the FD1 and FD2 mutations.

The Examiner also states that claims 66 and 67 are not entitled to the filing date of the provisional application 60/260,080 because the application does not appear to specifically disclose kits which amplify a region extending from the beginning of exon 18 or 19 through exon 23 of SEQ ID NO:1.

Applicants have canceled claims 50, 65-67, and 76-80. However, Applicants contend that all claims of the instant application as added herein by amendment are entitled to the priority of provisional application 60/260,080, as they all have a clear basis in that application.

As an initial matter, the Examiner alleges that SEQ ID NO:2 is not entitled to the benefit of priority of the provisional application. Applicants assert that SEQ ID NO:2 is entitled to the benefit of the provisional application; however, to advance prosecution, the claims of the instant application do not include SEQ ID NO:2.

The provisional application describes what is essential for carrying out the invention, and conveys that the inventors possessed the invention as of the filing date of the provisional application, and based on the disclosure of the provisional, one skilled in the art at that time would have been able to practice the claimed invention. The provisional application discloses the major and minor FD mutations, making clear that Applicants were in possession of the location of the major and minor FD mutations. The provisional application describes on page 2, lines 27-29 - page 3, lines 1-2, that the mutation associated with the major haplotype is a T-C change located at base pair 6 of intron 20 of the IKBKAP gene, and that the mutation associated with the minor haplotype is a G-C change located at base pair 73 of exon 19.

The provisional application discloses the claimed oligonucleotide probes and PCR primers for the detection of mutations of the FD gene. As stated on page 13, lines 27-29 - page 14, lines 1-2 of the provisional application: "Design and selection of suitable probes and primers is routine for the skilled worker. For example, suitable probes for detecting a given mutation include the nucleotide sequence at the mutation site and encompasses a sufficient number of nucleotides to provide a means of differentiating a normal from a mutant allele." Thus, the provisional application discloses the FD mutations and primers and probes used for detecting them.

The Examiner contends that certain of the claims do not enjoy the benefit of the provisional application because allegedly, according to the Examiner, it was not filed with a complete set of drawings and disclosed the first 53,050 bases of the 66,476 base long IKBKAP genomic sequence. However, the pending claims are entitled to the benefit of the provisional application whether or not the last 13,426 bases of SEQ ID NO:1 were disclosed. This is because the 53,050 bases the Examiner acknowledges were included in the is more than sufficient to cover the PCR primers and oligonucleotide probes recited in the claims. In particular, the claims recite probes suitable for detection of FD mutations, and kits containing a pair of PCR primers to amplify the FD mutation region. As described in the provisional application and recognized in the art, these primers and probes are chosen within close proximity of the mutation sites which are at positions 33,714 and 34,201, more than 20,000 base pairs from the end of the sequence in the provisional application. Thus, those skilled in the art would recognize that the recited primers and probes would be derived from sequences within tens or at most hundreds of base pairs from the mutations. The provisional application teaches that the probes may be 16 or 18 nucleotides and that the PCR primers flank the mutation site and would

not be greater than 20,000 bases from it. Accordingly, the claimed primers and probes are well within the 53,050 bases of the portion of SEQ ID NO:1 that were unequivocally provided in the provisional application.

Further, on page 14, the provisional application states that production of the PCR primers and oligonucleotide probes of the invention can be carried out by routine methods such as those in WO 93/06244 (to the Scripps Research Institute) ("Scripps publication") which is directed to the detection of mutations associated with Goucher's disease. The Scripps publication teaches that their probes are capable of hybridizing to nucleotide sequences that are preferably at least 10 nucleotides in length, and most preferably 17 nucleotides in length (at page 18). The preferred PCR primers of the Scripps publication, which are for the detection of an insertion mutation of one nucleotide (see page 7), are both 19 nucleotides in length (at page 30). These routine methods and references in the provisional application lend further support that the oligonucleotide probes and PCR primers of the instant invention are on the order of tens of bases, and for the efficacy of PCR, the primers are much closer than 20,000 bases to the mutation site, as they are for the detection of single nucleotide FD mutations.

In addition, claims 81-92, 94, 96, and 98-101 claim probes comprising 16 nucleotides or consisting of 16 nucleotides of SEQ ID NO:1 and containing the position of one of the FD mutations are also supported by the provisional application because the portion of SEQ ID NO:1 in the provisional application that the Examiner acknowledges was present, includes 16 nucleotides on either side of position 33,714 and 33,201 (in fact, kilobases more than that).

Claims reciting probes consisting of at least 16 contiguous nucleotides of exon 20 and intron 20 or exon 19 and intron 19 of SEQ ID NO:1 are likewise supported by the provisional application. As discussed above, the provisional application discloses probes that can be used to

detect, i.e., hybridize to, a nucleotide sequence containing position 34,201 which, as disclosed in the provisional application, is in intron 20, 6 bases from the border of exon 20 and intron 20. Thus, the provisional application discloses probes within exon 20 and intron 20. The provisional also discloses probes that can be used to detect a nucleotide sequence containing position 33,714, which as disclosed in the provisional application, is in base pair 73 of exon 19. Figure 1 of the provisional depicts the introns and exons of the genomic sequence of the IKBKAP gene (i.e., SEQ ID NO:1). Figure 1 thus discloses the intron and exon segments of the IKBKAP genomic sequence. Although the exact intron-exon boundaries are not provided in Figure 6 depicting the IKBKAP genomic sequence, from the disclosed position of the mutations within the intron or exon and by comparison with the IKBKAP protein coding sequence of which was known (see Cohen, of record), one skilled in the art could identify the distal borders of exon 20 and intron 20 (the border between the two segments being disclosed as 6 bases from position 34,201) and of intron 19 and exon 19 (the border between the two being disclosed as 73 bases from position 33,714). Thus, the provisional discloses the introns and exons of the IKBKAP genomic sequence and PCR primers and oligonucleotide probes therein. Accordingly, such claims are supported in the provisional application.

Thus, based on the arguments above, Applicants submit that the instant claims should have the benefit of the provisional application filed January 6, 2001. Because the claims deserve the benefit of the priority application they are not anticipated by the Slaugenhaupt, Rubin, Anderson, Gill, or Slaugenhaupt GenBank references cited by the Examiner; however, as detailed below, Applicants have provided additional bases for finding that these references do not anticipate the claims. Applicants, however, respectfully request acknowledgement by the Examiner that the instant claims deserve the benefit of the priority application.

35 U.S.C. § 112, first paragraph, written description

Claims 65-67, 77, and 79 are rejected under 35 U.S.C. § 112, first paragraph for failing to comply with the written description requirement. Applicants respectfully traverse.

The Examiner states on pages 5-18 of the Office Action that the specification as filed does not appear to provide support for the rejected claims. The Examiner states on page 8 of the Office Action, however, that the rejection can be overcome by amending the claims to recite that the nucleotide sequences recited are contiguous nucleotide sequences of SEQ ID NO:1. Claims 65-67, 77, and 79 are canceled. To advance prosecution, new claims 81-92, 94, 96, and 98-101 all recite that the claimed primers and probes have a contiguous nucleotide sequence of SEQ ID NO:1 as suggested by the Examiner. Therefore, the rejection is now moot and Applicants respectfully request that the rejection under 35 U.S.C. § 112, first paragraph be withdrawn.

35 U.S.C. § 102

Claims 77 and 78 are rejected under 35 U.S.C. § 102(b) as being anticipated by Cohen (U.S. Patent No. 5,891,719). Claims 77 and 78 are canceled. Applicants submit that the pending claims are not anticipated by Cohen. Cohen does not teach a nucleic acid sequence containing the mutation at positions 33,714 or 34,201 of SEQ ID NO: 1 of the instant application, nor does Cohen teach kits containing oligonucleotide probes that contain either of those mutations or PCR primers to specifically amplify the region containing the FD mutations. In addition, Cohen does not disclose the genomic sequence of the IKBKAP gene and, thus, does not disclose the sequence of intron 20, the location of position 34,201. In addition, Cohen does not teach that mutations at positions 33,714 or 34,201 are associated with FD. Accordingly,

Cohen does not anticipate or render obvious the claimed probes and kits useful for detecting the FD mutations.

Claims 77-80 are rejected under 35 U.S.C. § 102(a) as being anticipated by Rubin (2002/0168656), claims 77-80 are rejected under 35 U.S.C. § 102(a) as being anticipated by Anderson (Amer. J. Hum. Gen., 2001), and claims 77-79 are rejected under 35 U.S.C. § 102(a) as being anticipated by Slaugenhaupt (Amer. J. Hum. Gen., 2001). Claims 77-80 are now canceled. As an initial matter, Applicants point out that the Rubin reference could not be 102(a) art because it published on November 14, 2002, which is after the filing date of the instant application. Applicants assume that the Examiner intended to use the Rubin reference as §102(e) art.

Applicants respectfully submit that the pending claims are not anticipated by the Rubin, Anderson, or Slaugenhaupt references.

First, Applicants assert that, for the reasons set forth above, the pending claims are entitled to priority of provisional application 60/260,080, which was filed on January 6, 2001, which antedates all of these references and, thus, the references are not prior art. Alternatively and to expedite prosecution, however, Applicants submit herewith a Declaration of the Inventors Under 37 C.F.R. §1.131 ("the 131 Declaration") which demonstrates that the named inventors of the instant application conceived of and reduced to practice at least one embodiment of the claimed invention (or conceived of and reduced to practice that which would have rendered the invention obvious) prior to the references cited by the Examiner.

In particular, the 131 Declaration provides evidence that the inventors, Drs. Gusella and Slaugenhaupt, had identified the mutations at positions 33,714 and 34,201 prior to the effective dates of the above-listed references and had identified these mutations in samples from FD

carriers (131 Declaration, paragraph 5). Once these mutations had been identified, it was obvious and routine to produce and use PCR primers and oligonucleotide probes to detect these mutations in samples based upon nucleic acid diagnostic technology available at that time. Thus, by identifying the mutations, the inventors had reduced to practice an embodiment that rendered the claimed invention obvious. Thus, the Rubin, Anderson, and Slaugenhaupt references do not anticipate the pending claims because they were published within a year of the latest possible effective filing date of the claims (although Applicants submit that the claims deserve the benefit of the provisional application) and after the inventors made the claimed invention.

Further, with respect to Slaugenhaupt, Applicants submit herewith a Declaration of the Inventors Under 37 C.F.R. §1.132 ("the 132 Declaration") supporting that the inventors of the instant application, Susan A. Slaugenhaupt and James F. Gusella, are also authors on the Slaugenhaupt reference, and that they are properly the only two named inventors on the application relative to the Slaugenhaupt reference which names a number of other authors. In the 132 Declaration, inventors Gusella and Slaugenhaupt describe the roles of the other authors of Slaugenhaupt that are not named as inventors of the present application. Because, as detailed in the 132 Declaration, the other authors (1) worked as technicians or postdoctoral fellows carrying out experiments either related to the research described in Slaugenhaupt but not to the conception of the claimed invention, or (2) conducted experiments at the direction of Drs. Slaugenhaupt or Gusella, or (3) provided clinical samples, or reagents, or (4) sequenced samples provided by Dr. Slaugenhaupt at her direction, only Drs. Slaugenhaupt and Gusella made an inventive contribution to the claimed invention (132 Declaration at paragraphs 4-8). Accordingly, the subject matter disclosed in Slaugenhaupt is the inventors' own work and is not "by another." As

such, Slaugenhaupt is not prior art to the presently claimed invention and cannot anticipate the claims.

Claim 78 is rejected under 35 U.S.C. § 102(a) as being anticipated by Slaugenhaupt (GenBank Acc. No. AF153419). Claim 78 is now canceled. Applicants assert that this reference does not anticipate the claims of the instant invention. First, Applicants assert that they are entitled to priority to provisional application 60/260,080, which was filed on January 6, 2001 which antedates this reference. Further, this Slaugenhaupt GenBank reference (which has a subset of the authors of Slaugenhaupt discussed above) cannot be prior art because it is not by another for the same reasons discussed above with respect to Slaugenhaupt based upon the 132 Declaration. In addition, the 131 Declaration shows that the invention had been made prior to the publication of the Slaugenhaupt Genbank reference, and thus is not prior art to it. For all these reasons, the Slaugenhaupt Genbank publication does not anticipate any of the claims.

Claim 78 is also rejected under 35 U.S.C. § 102(b) as being anticipated by Gill (GenBank Acc. No. AF153419). The Examiner states the Gill reference teaches that position 2397 of the IKBKAP cDNA sequence (SEQ ID NO:2 of the instant application) contains a polymorphism. Applicants note that Gill in fact does not teach that there is a polymorphism at this position, or at any position for that matter. Applicants respectfully direct the Examiner to the Office Action of December 1, 2004, in which the Examiner states that "[t]he cDNA of Gill includes nucleotide position 2397 and hybridizes with IKBKAP nucleic acids comprising the 2397 FD mutation" and to the copy of Gill attached thereto which clearly does not teach that there is any variation at that position. Gill, therefore, does not teach a nucleic acid sequence containing the mutation at positions 33,714 or 34,201 of SEQ ID NO:1 of the instant application, nor does Gill teach or suggest kits containing oligonucleotides that contain either of those mutations. Thus, even if Gill

were prior art (which it is not), Gill does not anticipate or render obvious the claimed invention. In addition, Gill lists as authors the inventors plus a subset of the authors on the Slaugenhaupt publication and for the same reasons discussed above with respect to Slaugenhaupt based upon the 132 Declaration Gill is not by another. In addition, the 131 Declaration shows that the invention had been made prior to the publication of the Gill reference, and thus is not prior art to it. Because the Gill reference is not prior art, the reference does not anticipate the claimed invention under §102(a).

Claims 50 and 76-80 are rejected under 35 U.S.C. § 102(a) as being anticipated by Boehringer Mannhein (Biochm. Mol. Biol., 2001). Claims 50 and 76-80 are now canceled. Applicants assert that this reference does not anticipate the claims of the instant invention. The Examiner indicates on page 23 of the Office Action that these rejections can be overcome by amending the claims to recite that the claimed oligonucleotides have a nucleotide sequence of contiguous nucleotides of SEQ ID NO:1. To advance prosecution, Applicants have adopted the Examiner's suggestion and recite a contiguous nucleotide sequence of SEQ ID NO:1 in new claims 81-92, 94, 96, and 98-101. Therefore, the rejections are now moot and Applicants respectfully request that the rejections under 35 U.S.C. § 102 (a) and (b) be withdrawn.

35 U.S.C. § 103(a)

Claims 65-67 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Slaughenhaupt (Amer. J. Hum. Gen., 2001) in view of Fodor (U.S. Patent No. 5,968,740). Claims 65-67 are now canceled.

As discussed above, for a number of reasons Slaugenhaupt is not prior art to the claims of the instant invention. Fodor itself does not relate at all to FD mutations and, thus, does not

render the claims obvious. Applicants respectfully request that the rejections under 35 U.S.C. § 103 (a) be withdrawn.

CONCLUSION

Based on the foregoing remarks, Applicants respectfully request reconsideration and withdrawal of the rejection of claims and allowance of this application.

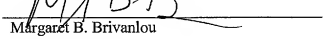
AUTHORIZATION

The Commissioner is hereby authorized to charge any additional fees which may be required for consideration of this Amendment to Deposit Account No. 50-3732, Order No. 13572.105039.

In the event that an extension of time is required, or which may be required in addition to that requested in a petition for an extension of time, the Commissioner is requested to grant a petition for that extension of time which is required to make this response timely and is hereby authorized to charge any fee for such an extension of time or credit any overpayment for an extension of time to Deposit Account No. 50-3732, Order No. 13572.105039

Respectfully submitted,
KING & SPALDING LLP

Dated: February 28, 2007
By:



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